IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE APPLICATION OF:	KOLTER ET AL.	DOCKET NO.:	51497
SERIAL NO.	09/873,431	CONFIRMATION NO.:	5147
FILED:	JUNE 05, 2001	GROUP ART UNIT:	1618
FOR:	A PROCESS FOR PRODUCING SOLID ORAL DOSAGE FORMS WITH SUSTAINED RELEASE OF ACTIVE INGREDIENT	EXAMINER:	B. M. FUBARA

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. ☐ NOTICE OF APPEAL: Applicant hereby appeals to the Board of Appeals from the decision dated -/-, of the Primary Examiner finally rejecting Claims -/-.
2. ☒ BRIEF ON APPEAL in this application is transmitted herewith.
   ☐ Appellants hereby request an Oral Hearing.
3. ☒ Appellants hereby request entry of their timely reply dated *June 08, 2007,* for purposes of appeal.
4. ☐ Appellants hereby petition for a -/- month extension of time under 37 C.F.R. §1.136(a).
   ☐ A petition for a -/- month extension of time including the requisite fee of -/- has been submitted along with the reply under 37 C.F.R. §1.116 dated -/-.
5. ☒ The following fee(s) in the total amount of **-$500.00-** is(are) paid herewith by credit card (Form PTO-2038 enclosed):
   ☒ The *$ 500.00* fee required under 37 C.F.R. §41.20(b)(2).
   ☐ The -/- fee required under 37 C.F.R. §41.20(b)(3).
   ☐ The -/- fee required under 37 C.F.R. §1.17(a).
   ☐ A fee is not required (Fee paid in prior appeal).
6. ☒ The Commissioner is hereby authorized to charge any fee which may be further required, or credit any over payment, to Deposit Account No. 14.1437. A duplicate copy of this sheet is attached.

Respectfully submitted,
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Honorable Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

BRIEF ON APPEAL UNDER 37 C.F.R. §41.37

Sir:

This is an appeal from the Examiner's final rejection of Claims 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33, dated February 27, 2007. Claims 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33 are currently pending.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account No. 14.1437. Please credit any excess fees to such deposit account.

Respectfully submitted,
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JR/BAS

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Real Party in Interest

The real party in interest is BASF Aktiengesellschaft, 67056 Ludwigshafen, Germany.

Related Appeals and Interferences

To the best of the undersigned's knowledge, there are no related appeals or interferences within the meaning of 37 C.F.R. §41.37(c)(1)(ii).

Status of the Claims

The claims on Appeal before the Board of Patent Appeals and Interferences are Claims 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33. A copy of these claims is found in the attached Claims Appendix. The status of the claims is as follows:

- Claim(s) 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33 is(are) pending;
- Claim(s) 10, 11, 14, 15, 24 and 26 is(are) canceled;
- Claim(s) 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33 is(are) rejected;
- Claim(s) -/- is(are) allowed;
- Claim(s) -/- is(are) withdrawn; and
- Claim(s) -/- is(are) objected to.

Status of the Amendments

The claims as currently pending were presented with appellants' paper dated February 16, 2006, in reply to a non-final Office action dated September 27, 2005, and were resubmitted on May 11, 2006. No further amendments were filed subsequent to the final Office action dated February 27, 2007.

Summary of the Claimed Subject Matter

Claims 1, 17, and 25 are independent and/or will be argued separately in this paper. Claims 2 to 9, 12, 13, 16, and 27 to 32 depend either directly or indirectly upon Claim 1, and Claims 18 to 23, and 33 depend either directly or indirectly upon Claim 17. These claims are not being argued separately. A summary of the respective embodiments of appellants' invention is therefore deemed to be unnecessary.[1)]

In a first aspect which is set forth in Claim 1, appellants' invention pertains to a certain pro-

1) 37 C.F.R. §41.37(v).

cess for producing a particular oral dosage form with sustained release of active ingredient.[2] The particular dosage form comprises

a) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone which acts as a binder and a matrix former,[3] and wherein the polyvinylpyrrolidone has a molecular weight of from 20,000 to 1,000,000, and the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate,[4]

b) at least one active ingredient,[5]

c) optionally water-soluble polymers or low or high molecular weight lipophilic additives,[6]

d) and, optionally, excipients,[7]

and the process entails granulating a mixture of (a) and (b) and optionally (c) and/or (d) by heating said mixture to a temperature of from 40°C to 130°C,[8] in the absence of solvents.[9]

Appellants' process applies the principle of melt granulation, wherein the formulated mixture (a) acts both as binder and as matrix former. However, no melt is present in the granulation.[10] Therefore, adhesion effects and accretions on mixer implements or mixer walls during the process are avoided.[11] Upon granulating the mixture of (a) and (b) and optionally (b) and/or (c) in accordance with appellants' process, granules are formed which comprise the active ingredient(s) (b) and, where present, component(s) (c) and/or (d), with the formulated mixture (a) acting as a binder and matrix former. Notably, a granulate of (a) and (b) which is obtained in accordance with appellants' process exhibits properties which are distinctly different from the properties of a physical mixture of the components (a) and (b).[12]

Due to the use of the formulated mixture (a) in combination with the active ingredient(s) (b) and optionally component(s) (c) and/or (d) in appellants' process it is possible to obtain a granulate of the active ingredient(s) in a "one-pot system" and in the absence of any solvents. As illustrated,

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2) Cf., e.g., page 1, indicated lines 5 to 13, and page 4, indicated line 36, to page 5, indicated line 4, of the application.

3) Cf., e.g., page 5, indicated lines 6 to 8, of the application.

4) Cf., e.g., page 8, indicated lines 36 to 46, of the application.

5) Cf., e.g., page 5, indicated lines 15 to 18, page 9, indicated line 42, to page 10, indicated line 38, of the application.

6) Cf., e.g., page 6, indicated line 19, to page 8, indicated line 34, of the application.

7) Cf., e.g., page 9, indicated lines 7 to 40, and page 11, indicated lines 12 to 15, of the application.

8) Cf., e.g., page 5, indicated lines 28 to 45, of the application.

9) Cf., e.g., page 11, indicated lines 19 to 20, of the application.

10) Cf., e.g., page 5, indicated lines 6 to 15, of the application.

11) Cf., e.g., page 6, indicated lines 4 to 17, of the application.

12) Cf., e.g., the flow properties set forth in Table 1 on page 12 of the application, and the active ingredient release properties set forth in Table 8 on page 18 of the application.

for example, in Table 1,[13] the granules obtained in accordance with appellants' process exhibit significantly improved flow properties when compared to a physical mixture of the constituents, and to granules prepared with the aid of conventional binders such as Metocel K 15M[14] or stearyl alcohol.

Moreover, appellants' process is in principle independent of the physico-chemical properties of the active ingredient, i.e. the active ingredient may be water-soluble, water-insoluble, acidic or basic, or low-melting.[15] A particular advantage of appellants' process is also that even active ingredients whose tablettability is known to be poor can be processed in a simple manner.[16]

A second aspect of appellants' invention is defined in Claim 17 which pertains to an oral dosage form[17] which comprises

a) the formulated mixture of polyvinyl acetate and polyvinylpyrrolidone which acts as a binder and a matrix former,[3] and wherein the polyvinylpyrrolidone has a molecular weight of from 20,000 to 1,000,000, and the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate,[4]

b) at least one active ingredient,[5]

c) optionally water-soluble polymers or low or high molecular weight lipophilic additives,[6]

d) and, optionally, excipients,[7]

wherein the process comprises granulating a mixture of (a) and (b) and optionally (c) and/or (d) by heating it to a temperature of from 40°C to 130°C.[8] In addition to the advantages which arise due to simplified processing in accordance with appellants' invention,[18] the dosage form which is produced from the granules obtained in accordance with appellants' process exhibits increased hardness.[19] It is, therefore, unnecessary to carry out an additional thermal after-treatment, or to apply an additional coating to the tablets,[20] to harden or otherwise protect the dosage form. Moreover, the release of the active ingredient from appellants' dosage form is sustained for a significantly longer period of time than the release of active ingredient from tables made with conventional binders such as Metocel K 15M[14] and stearyl alcohol.[18] Notably, the release of the active ingredient from appellants' dosage form is also sustained for a significantly longer period of time than the release of active ingredient from a tablet made by compressing a physical mixture of the

13) Cf., e.g., page 12, indicated lines 1 to 19, of the application.

14) A hydroxymethylcellulose; cf., e.g., page 19, indicated lines 15 to 29, of the application.

15) Cf., e.g., page 5, indicated lines 15 to 18, of the application.

16) Cf., e.g., page 11, indicated lines 23 to 34, and page 13, indicated lines 1 to 4, of the application.

17) Cf., e.g., page 5, indicated lines 20 to 26, page 9, indicated lines 1 to 5, and page 10, indicated line 40, to page 11, indicated line 10, of the application.

18) Cf., e.g., page 20, indicated line 1, to page 21, indicated line 30, of the application.

19) Cf., e.g., page 12, indicated line 21, to page 13, indicated line 10, of the application.

20) Cf., e.g., page 11, indicated lines 17 to 23, of the application.

active ingredient (b) and the formulated mixture (a).[21)]

In a third aspect which is defined in Claim 25, appellants' invention pertains to a method of delaying the release of at least one active ingredient. The method entails producing the oral dosage form of Claim 17. Additionally, Claim 25 sets forth that the at least one active ingredient comprises food supplements or additives, vitamins, minerals or trace elements.[22)]

GROUND(S) OF REJECTION TO BE REVIEWED

I) Whether the Examiner erred finding that the subject matter of appellants' Claims 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33 was *prima facie* obvious under 35 U.S.C. §103(a) in light of the teaching of ***Ortega et al.*** **(US 4,837,032)**.

II) Whether the Examiner erred finding that the subject matter of appellants' Claims 1 and 8 was *prima facie* obvious under 35 U.S.C. §103(a) in light of the teaching of ***Ortega et al.*** **(ibid.)** when taken in view of the disclosure of ***Noda et al.*** **(US 5,389,380)**.

ARGUMENT(S)

GENERAL CONSIDERATIONS

The United States Supreme Court held in *Graham v. John Deere* that:[23)] *"Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."* Thus, four factual inquires must be addressed to determine obviousness:

(A) the scope and contents of the prior art;

(B) the differences between the prior art and the claims in issue;

(C) the level of ordinary skill in the pertinent art; and

(D) evidence of secondary considerations.

When the scope and the contents of the prior art is determined, it is *inter alia* necessary that the references be considered as a whole, and that the references be viewed without the benefit of imper-

21) Cf., e.g., the active ingredient release properties set forth in Table 8 on page 18 of the application.

22) Cf., e.g., Claim 17 in conjunction with page 10, indicated lines 1 to 3, of the application.

23) *Graham v. John Deere*, 383 U.S. 1, at 17 - 18, 148 USPQ 459 (1966).

missible hindsight vision afforded by the claimed invention.[24] Recently addressing the issue of obviousness, the United States Supreme Court further explained:[25] "*Often, it will be necessary ... to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine known elements in the fashion claimed by the patent at issue.*" Accordingly, obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination.[26] It is insufficient that the prior art discloses the components of the claimed invention, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination that was made by the inventor.[27]

To render the claimed combination of elements obvious it is necessary that there be evidence of a motivating force which would impel a person skilled in the art to do what the applicant has done. The mere fact that the prior art could be combined and/or modified so as to arrive at the applicant's invention as claimed does not suffice to render such a modification *prima facie* obvious unless the prior art suggests the desirability of the modification.[28] Also, the fact that the respective combination and/or modification is within the skill in the art does not allow a conclusion that the prior art provides for a motivation to make the pertinent combination and/or modification.[29] "Would have been able to produce" does not meet the standards applicable to a determination under Section 103(a).[30] The United States Supreme Court also cautioned:[31] "*rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.*"

I) *The Examiner's finding that the subject matter of appellants' Claims 1 to 9, 12, 13, 16 to 23, 25 and 27 to 33 was* prima facie *obvious under 35 U.S.C. §103(a) in light of the teaching of* **Ortega**

24) *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

25) *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007), Slip op. at 14.

26) *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 466 (Fed. Cir. 1986); *In re Laskowski*, 871 F.2d 115, 10 USPQ2d 1397 (Fed. Cir. 1989).

27) *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 15 USPQ2d 1321 (Fed. Cir. 1990), *cert. denied* 498 U.S. 920 (1990).

28) Cf. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); see also, e.g., *Interconnect. Planning Corp. v. Feil*, 774 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985); *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983).

29) Cf. *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998); *Al Site Corp. v. VSI International, Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

30) *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986).

31) *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007), Slip op. at 14.

et al. *is, for the following reasons, deemed to be in error.*

When the teaching of ***Ortega et al.*** is considered as a whole, without the benefit of impermissible hindsight vision afforded by appellants' invention, the reference clearly fails to suggest the desirability and thus the obviousness of making the combination which is required by the claimed invention. The reference also fails to teach or suggest all of the elements of appellants' claims, and fails to provide the suggestion or motivation which was necessary for a person of ordinary skill to produce an oral dosage form with sustained release of active ingredient in accordance with appellants' invention.

The teaching of ***Ortega et al.*** pertains to the preparation of theophylline tablets which exhibit a sustained release of the active ingredient, i.e. theophylline is released such that relatively uniform blood levels are achieved.[32] The controlled steady release is achieved by means of a polymeric matrix composed of

- from 10 to 20 weight percent of water insoluble polymer which serves as a retardant against drug dissolution, e.g. polymers which are not digested as they pass the gastro-intestinal tract such as polyvinyl acetate, polyvinyl alcohol, vinyl chloride/vinyl acetate copolymers, acrylate polymers and copolymers, methacrylate polymers and copolymers, copolymers of ethyl methacrylate and copolymers of methyl methacrylate, preferred being polyvinyl acetate (*in the following also abbreviated as* **PVAc**);[33]
- from 5 to 15 weight percent of acid insoluble polymer having carboxylic groups, which retards drug dissolution in the stomach while allowing dissolution in intestinal fluid, such as cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, esters of acrylic acid copolymers and esters of methacrylic acid copolymers, preferably cellulose acetate phthalate,[34] and
- from 10 to 15 weight percent of water soluble polymers or hydrophobic gel forming polymers which swell or dissolve in water, and thereby permit the controlled drug dissolution as the gastro-intestinal fluids penetrate and erode the tablet, such as polyvinylpyrrolidone, or cellulose derivatives such as hydroxypropyl methyl cellulose, methyl cellulose or sodium carboxy methyl cellulose, preferably polyvinylpyrrolidone (*in the following also abbreviated as* **PVP**).[35]

According to the authors, the composition causes the tablet to swell and slowly erode rather than disintegrating. Erosion proceeds for an extended period of time with release of theophylline by a

32) Col. 1, indicated lines 5 to 8, and col. 2, indicated lines 51 to 55, of ***US 4,837,032***.

33) Col. 3, indicated line 5, indicated lines 11 to 12, and indicated lines 27 to 38, of ***US 4,837,032***.

34) Col. 3, indicated lines 9 and 10, indicated lines 12 to 14, and indicated lines 38 to 48, of ***US 4,837,032***.

35) Col. 3, indicated lines 6 to 8, indicated lines 14 to 17, and indicated lines 48 to 55, of ***US 4,837,032***.

diffusion process. The tablet disintegrates into particles only after several hours.[36] The tablets are prepared by:[37]

compounding the theophylline with the acid insoluble polymer, preferably to a particle size of less than 30 mesh.

*The resulting mixture may then be blended and wet granulated with a portion of the film former [*inter alia PVP*] in a solution such as ethyl alcohol in the case of polyvinylpyrrolidone.*

The granulate may then be sized through a sieve, optimally 16 mesh,
*mixed with the remaining film former [*inter alia PVP*], the insoluble polymer [*inter alia PVAc*] (also optimally powdered to less than 30 mesh) and the lubricant.*

The resulting mixture may then be compressed using a standard rotary tablet press.

Additionally, the reference provides in the context of illustrative Example 1:[38] "*The dried granulate [of theophylline, cellulose cetate phthalate and polyvinylpyrrolidone] was sized through a 16 mesh sieve, and then transferred to a V-blender. 9 kg of polyvinyl acetate (particle size less than 30 mesh) was added plus 6 kg of polyvinylpyrrolidone and 3 kg of the lubricant mix (stearic acid: talc: magnesium stearate 3:1:0.5). All the ingredients were mixed for 20 minutes. The granulate so obtained was compressed into tablets ...*"

CONCERNING THE PROCESS OF CLAIM 1:

The Examiner argued:[39] "*It is this dried theophylline based product [*obtained after drying the granulate*] that is combined with PVP and PVA and lubricant and the granules from this step are formulated into tablets. ... Therefore, Ortega discloses the process of claim 1 with respect to the process where 1 a) and 1 b) are granulated. Ortega does not indicate that solvent is used in the second step. The claim does not state any particular order of adding the components. Therefore, with respect to applicant's argument, Ortega discloses all the elements of the claims as described above.*"

It is respectfully urged, however, that that the stage of ***Ortega et al.***'s process in which the dried granulate is "*mixed with the remaining film former [*inter alia PVP*], the insoluble polymer [*inter alia PVAc*] (also optimally powdered to less than 30 mesh) and the lubricant*"[40] cannot reasonably be regarded to suggest or imply a granulation as is required in accordance with the provisions of appellants' claims. The statements made in col. 4, indicated lines 4 to 10, of the reference clearly show that the authors distinguish between granulating and mixing as procedural measures.

36) Col. 2, indicated lines 56 to 63, of ***US 4,837,032***.
37) Col. 4, indicated lines 1 to 13, of ***US 4,837,032***.
38) Col. 4, indicated lines 34 to 42, of ***US 4,837,032***.
39) Final Office action page 7, lines 4 to 11.
40) Col. 4, indicated lines 7 to 10, of ***US 4,837,032***.

The same distinction is made by the authors in the description of the illustrative example which, on the one hand, explains that "*A mixture of ... was granulated ...,*" and, on the other hand, notes that "*All ingredients were mixed for 20 minutes.*" As such, the reference merely provides that the granulate obtained in the first stage be mixed with certain further particulate components. Necessarily, the product which is obtained by mixing the components with one another has the form of a granulate. This does, however, not per se mean that the mixing step causes the particles which are being mixed to interact such that granules are formed which comprise all of the mixed components. In other words, mixing does not per se mean that granulating takes place.

In accordance with the illustrative procedure the following particulate components are dry-mixed for a period of 20 minutes:[41)]

- the dried granulate of theophylline, polyvinylpyrrolidone and cellulose cetate phthalate sized through a 16 mesh sieve;
- polyvinyl acetate having a particle size of less than 30 mesh;
- polyvinylpyrrolidone; and
- a stearic acid: talc: magnesium stearate lubricant.

Although not specifically mentioned in the reference it can reasonably be assumed that the **PVP** and the lubricant were also employed in particulate form. The resulting mixture necessarily has the form of a granulate. The statement of ***Ortega et al.*** that:[42)] "*The granulate so obtained was compressed into tablets ...*" can therefore not be deemed to suggest or imply that granulation takes place when the dried granulate, the **PVAc**, the **PVP**, and the lubricant are mixed for 20 minutes as the Examiner would have it.

It is further respectfully urged that the Examiner's argument fails to appreciate appellants' requirement that the mixture comprising (a) and (b) be granulated "*by heating to a temperature of from 40°C to 130°C in the absence of solvents.*" The teaching of ***Ortega et al.*** clearly fails to suggest or imply that the mixing step be conducted at an elevated temperature. ***Ortega et al.*** merely state that the polymers were added to a certain mixer and were mixed for 20 minutes. In contrast thereto, appellants' Claim 1 requires that the components be heated to a temperature of from 40 to 130°C for granulation. The Examiner asserted:[43)] "*Ortega discloses a process of wet granulating a mixture of theophylline, polyvinylpyrrolidone cellulose[,] acetate phthalate; the dried granulate is then combined with mixture of polyvinylpyrrolidone, polyvinyl acetate and lubricant, which is a mixture ... [of] stearic acid, magnesium stearate and talc (abstract; column 2, lines 56-68; column 3, lines 57-63; and column 4, lines 3-18) at a temperature of 40°C to 50°C (example 1).*" The

41) Col. 4, indicated lines 34 to 39, of ***US 4,837,032***.

42) Col. 4, indicated lines 39 to 42, of ***US 4,837,032***.

43) Final Office action page 4, lines 3 to 7; emphasis added.

Examiner's summary of the facts is, however, deemed to be incorrect and misleading. The temperature of 40°C to 50°C is employed by ***Ortega et al.*** to dry the product obtained in the initial wet granulation step:[44] "*... The wet mass was dried in a fluid bed dryer at 40°C-50°C. for 30 minutes. The dried granulate was sized ...*" The reference does not specify any particular temperature concerning the step of mixing the dried granulate with the other components.

Also, ***Ortega et al.*** neither teaches nor suggests that the dried granulate be combined with a "*mixture of polyvinylpyrrolidone, polyvinyl acetate and lubricant*" as the Examiner would have it. In the general description of the procedure, ***Ortega et al.*** state:[45] "*The [dried] granulate may then be seized through a sieve, ..., mixed with the remaining film former, the insoluble polymer (...), and the lubricant. The resulting mixture may then be compressed ...*" The description of illustrative Example 1 of the reference correspondingly sets forth:[46] "*The dried granulate was sized ..., and then transferred to a V-blender. 9 kg of polyvinyl acetate (...) was added plus 6 kg of polyvinylpyrrolidone and 3 kg of the lubricant mix (stearic acid: talc: magnesium stearate 3:1:0.5).*" The polyvinyl acetate and the polyvinylpyrrolidone which are employed in this stage of the prior art process are, accordingly, not mixed before they are added to the dried granulate, and the cited sections of the reference can clearly not suggest or imply a "*formulated mixture of polyvinyl acetate and polyvinylpyrrolidone ... wherein ... the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate,*" as required in accordance with appellants' component (a).

Additionally, the Examiner's argument fails to appreciate that appellants' process requires more than merely a combined use of PVP and PVAc. Appellants' component (a) is "*a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone which acts as a binder and a matrix former, and wherein ... the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate.*"[47] It is well known in the chemical art that a dispersion is a two phase system where one phase consists of finely divided particles (often in the colloidal size range) distributed throughout a bulk substance, the particles being the disperse or internal phase and the bulk substance being the continuous or external phase.[48] ***Ortega et al.***'s second step entails, as noted above, that polyvinylpyrrolidone and polyvinyl acetate be mixed for a period of 20 minutes. It is well known in the pertinent art that PVP and PVAc are not miscible with one another so that a simple combination of the polymers, even by way of a homogeneous melt, is not possible.[49]

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44) Col. 4, indicated lines 29 to 34, of ***US 4,837,032***.

45) Col. 4, indicated lines 7 to 11, of ***US 4,837,032***.

46) Col. 4, indicated lines 33 to 38, of ***US 4,837,032***.

47) Cf. Claim 1, emphasis added.

48) Cf., e.g., ***Hawley's*** Condensed Chemical Dictionary, 13th Ed. 1997, page 417.

49) Cf., e.g., ***Kolter et al.***, col. 2, indicated lines 57 to 60, of ***US 6,066,334***.

The combined utilization of the distinct polymers which is employed in procedure of ***Ortega et al.*** can, therefore, clearly not be deemed to correspond to, or to teach, suggest or imply, the particularities of, the formulated mixture which employed as component (a) in accordance with appellants' process. Merely mixing the polymers, as is done in accordance with the teaching of ***Ortega et al.*** cannot reasonably be considered to form a formulated mixture of PVP and PVAc in which finely divided particles of PVP are dispersed throughout a continues phase of the PVAc. Moreover, the fact that ***Ortega et al.*** dry-mix a combination of a granulate and other particulate components to obtain a granulate clearly fails to suggest or imply that the respective stage of the prior art example corresponds to a "granulation" as conducted in accordance with appellants' process.

The Examiner took the position:[50] "*The claim does not state any particular order of adding the components.*" Appellants respectfully disagree. Appellants' Claim 1 requires that component (a) be a certain "*formulated mixture of polyvinyl acetate and polyvinylpyrrolidone.*" It is therefore clearly required that the constituents of appellants' component (a) be present in the form of said formulated mixture before the component is granulated with the active ingredient (b) and optionally one or more of the further components (c) and/or (d).

For at least the foregoing reasons, the Examiner's position that ***Ortega et al.*** disclose all of the elements of appellants' Claim 1 is deemed to be in error. The teaching of ***Ortega et al.*** is in light of the foregoing remarks not deemed to be suited to establish that the subject matter of Claim 1 is unpatentable under Section 103(a).

CONCERNING THE DOSAGE FORM OF CLAIM 17:

The Examiner pointed out:[51] "*how the composition is made carries no patentable weight because product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps; and 'even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.'*" In other words: the manipulations per se have no limiting effect on a product which is defined in terms of product-by-process claim; however, the structure which is implied by the steps has to be taken into consideration when patentability is determined. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes,

50) Final Office action page 7, line 9.

51) Final Office action page 3, line 17, to page 4, line 3.

a prima facie case of either anticipation or obviousness has been established.[52] Appellants respectfully urge that those circumstances are not applicable in the present case.

As already explained in the discussion regarding Claim 1, the ***Ortega et al.*** reference fails to teach or suggest a dry-granulating step employing the active ingredient(s) and a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone wherein the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate. It has also been pointed out in that context that the mixture which is obtained in the second step of ***Ortega et al.***'s procedure by mixing a granulate comprising the active ingredient with polyvinylpyrrolidone and polyvinyl acetate for a period of 20 minutes, cannot reasonably be deemed to correspond to, or to teach, suggest or imply, the particularities of the formulated mixture which constitutes component (a) of appellants' dosage form. The fact that ***Ortega et al.*** dry-mix a combination of a granulate and other particulate components to obtain a granulate also, clearly fails to suggest or imply that the stage corresponds to a "granulation" as conducted in accordance with appellants' process. As such, the reference fails to teach or suggest all of the elements of appellants' claims, and fails to provide the suggestion or motivation which was necessary for a person of ordinary skill to modify the prior art tablets. Accordingly, the prior art process and appellants' process cannot be considered to be "*identical or substantially identical.*"

Additionally, considering the particularities of appellants' component (a), appellants' product cannot be deemed to be "*identical or substantially identical*" with the prior art tablet. As noted in the foregoing, ***Ortega et al.***'s procedure entails that a comminuted mixture of the active ingredient and the acid insoluble polymer is wet granulated with a film forming polymer such as polyvinylpyrrolidone, i.e. the active ingredient is brought into intimate contact with, or even embedded in, the acid insoluble polymer and/or the film forming polymer. Only after the product of the wet granulation has been dried and seized, the granules are mixed with further film former and with PVAc. This means that the product obtained in the procedure of ***Ortega et al.*** comprises the active ingredient primarily surrounded by the acid insoluble polymer and the film forming polymer.

Appellants' process comprises granulating the active ingredient with "*a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone ... wherein the polyvinylpyrrolidone ... is finely dispersed in the polyvinyl acetate,*" i.e. with a mixture in which the polyvinyl acetate constitutes the continuous or external phase in which the polyvinylpyrrolidone is dispersed.[4,48] This means that the granulating product which is obtained in accordance with appellants' process invention comprises the active ingredient primarily surrounded by, or even embedded in, the continuous polyvinyl acetate phase of the formulated mixture (a).

For at least the foregoing reasons, the Examiner's position that ***Ortega et al.*** disclose all of the elements of appellants' Claim 17 is deemed to be in error. The teaching of ***Ortega et al.*** is in

52) *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

light of the foregoing remarks not deemed to be suited to establish that the subject matter of Claim 17 is unpatentable under Section 103(a).

CONCERNING THE METHOD OF CLAIM 25:

The foregoing remarks are equally applicable where the subject matter of appellants' Claim 25 is concerned which pertains to a "*method of delaying the release of at least one active ingredient comprising producing the oral dosage form of claim 17 wherein the at least one active ingredient comprises food supplements or additives, vitamins, minerals or trace elements.*" (*emphasis added*). As emphasized in the foregoing partial reproduction of Claim 25, the pertinent elements of Claim 17, i.e. the components as well as the procedural measures which are required in accordance with appellants invention, are incorporated by reference.

According to the teaching of ***Ortega et al.*** the controlled steady release of theophylline is achieved by wet-granulating the active ingredient with the acid insoluble polymer and a film forming polymer, thereby forming a granulate in which the active ingredient is in intimate contact with, or even embedded in, the acid insoluble polymer and/or the film forming polymer. The procedure of ***Ortega et al.*** further entails that the granulate be mixed with further film-forming polymer, with the insoluble polymer, and with the lubricant, and that the resulting granulate be compressed into tablets.

As shown by appellants, the properties of a dosage form which is obtained by compressing a physical mixture of active ingredient (b) and the formulated mixture (a) differ considerably from the properties of a dosage form obtained by compressing a granulate obtained in accordance with appellants' process.[21)] Bearing in mind that PVP and PVAc are polymers which are not miscible with one another so that a simple combination of the polymers, even by way of a homogeneous melt, is not possible, it is immediately apparent that the release properties of a tablet which is obtained in the manner described by ***Ortega et al.*** by compressing a physical mixture of a theophylline granulate, PVP and PVAc cannot reasonably be considered to suggest the properties of a dosage form which is obtained in accordance with appellants' invention and in which the active ingredient is primarily surrounded by, or embedded in, a continuous polyvinyl acetate phase of the formulated mixture (a).

As such, the teaching of ***Ortega et al.*** is not deemed to be suited to establish that the subject matter of Claim 25 is unpatentable under Section 103(a).

II) *The Examiner's finding that the subject matter of appellants' Claims 1 and 8 was* prima facie *obvious under 35 U.S.C. §103(a) in light of the teaching of* **Ortega et al.** *when taken in view of*

the disclosure of **Noda et al.** *is, for the following reasons, deemed to be in error.*

The Examiner applied the secondary reference for teaching a theophylline composition which contains lactose or starch or mannitol excipient. ***Noda et al.***'s disclosure adds nothing to the teaching of ***Ortega et al.*** which could reasonably supplement the suggestion or motivation which is necessary for a person of ordinary skill in the art to modify ***Ortega et al.***'s tablets, or the process employed in accordance with ***Ortega et al.***'s teaching, as is necessary to arrive at the dosage forms, or the method or the process which is defined in appellants' claims. The disclosure of ***Noda et al.*** is equally unsuited to teach or suggest any of the limitations of appellants' claims which are missing from the teaching of ***Ortega et al.***

Even when the disclosure of ***Noda et al.*** is included in the consideration, at least two of the three basic criteria for establishing a prima facie case of obviousness are not met, and the references cannot reasonably be taken to establish that the subject matter of appellants' respective claims was prima facie obvious within the meaning of Section 103(a).

CONCLUSION

In light of the foregoing reasons and explanations as well as the explanations already presented by appellants in their papers dated February 16, 2006, and June 08, 2007,[53] appellants respectfully urge that the Examiner's rejections of appellants' claims under 35 U.S.C. §103(a) in light of the teaching of ***Ortega et al.*** when taken alone or taken in view of the disclosure of ***Noda et al.*** were in error. The Examiner's remarks are deemed to be mere conclusory statements which lack articulated reasoning with some rationale underpinning,[31] and are therefore not deemed to support the conclusion that the subject matter of appellants' claims was obvious under Section 103(a) in light of the referenced art. It is therefore respectfully requested that the Examiner's respective rejections be reversed. Favorable action is solicited.

53) The respective papers are herewith incorporated by reference.

CLAIMS APPENDIX:

1. A process for producing an oral dosage form with sustained release of active ingredient, wherein the dosage form comprises

   a) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone which acts as a binder and a matrix former, and wherein

   the polyvinylpyrrolidone has a molecular weight of from 20,000 to 1,000,000, and

   the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate,

   b) at least one active ingredient,

   c) optionally water-soluble polymers or low or high molecular weight lipophilic additives,

   d) and, optionally, excipients,

   wherein the process comprises granulating a mixture of a) to d) or a) to c) or a) and b) and d) or a) and b) by heating to a temperature of from 40°C to 130°C in the absence of solvents.

2. A process as claimed in claim 1, wherein the polyvinyl acetate to polyvinylpyrrolidone ratio is 6:4 to 9:1.

3. A process as claimed in claim 1, wherein the active ingredient : water-soluble polymers or low or high molecular weight lipophilic additives ratio employed is from 5:95 to 85:15.

4. A process as claimed in claim 1, wherein polyvinyl acetate and polyvinylpyrrolidone each have a molecular weight of from 20,000 to 1,000,000.

5. A process as claimed in claim 1, wherein the mixture is granulated by heating to from 45 to 100°C.

6. A process as claimed in claim 1, wherein the particle size of the active ingredients employed is in a range from 20 to 700 μm.

7. A process as claimed in claim 1, wherein the excipients employed are fillers, disintegrants and adsorbents, lubricants, flowability agents, dyes, stabilizers, antioxidants, wetting agents, preservatives, release agents, flavorings or sweeteners.

8. A process as claimed in claim 1, wherein fillers selected from the group consisting of lactose, cellulose powder, mannitol, calcium diphosphate and starch are employed as excipients.

9. A process as claimed in claim 1, wherein the granules can be produced by employing the process of mixer granulation, fluidized bed granulation or extrusion granulation.

12. A process as claimed in claim 1, wherein besides the formulated mixture of polyvinyl acetate and polyvinylpyrrolidone, further release-sustaining excipients may optionally be employed before, during or after the granulation.

13. A process as claimed in claim 1, wherein water-soluble, water-soluble highly swelling or lipophilic excipients are employed for further modification of release.

16. A process as claimed in claim 1, wherein the water-soluble polymers are selected from the group consisting of: polyvinyl alcohols, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones, vinyl acetate/vinyl pyrrolidone copolymers, polyethylene glycols, polyvinylpyrrolidones, vinyl acetate/vinylpyrrolidone copolymers, maltodextrins, and salts thereof.

17. An oral dosage form comprising

a) a formulated mixture of polyvinyl acetate and polyvinylpyrrolidone wherein the polyvinylpyrrolidone has a molecular weight of from 20,000 to 1,000,000, and the polyvinylpyrrolidone is finely dispersed in the polyvinyl acetate,

b) at least one active ingredient,

c) optionally water-soluble polymers or low or high molecular weight lipophilic additives, and

d) optionally, excipients,

wherein the mixture of a) to d) or a) to c) or a) and b) and d) or a) and b) is granulated by heating to a temperature of from 40°C to 130°C.

18. An oral dosage form as claimed in claim 17, which comprises as active ingredients food supplements or additives, vitamins, minerals or trace elements or active pharmaceutical ingredients.

19. An oral dosage form as claimed in claim 18, which comprises active pharmaceutical ingredients as active ingredients.

20. An oral dosage form as claimed in claim 18, wherein the active pharmaceutical ingredient is selected from the group consisting of benzodiazepines, antihypertensives, vitamins, cytostatics, anesthetics, neuroleptics, antidepressants, antibiotics, antimycotics, fungicides, chemotherapeutics, urologicals, platelet aggregation inhibitors, sulfonamides, spasmolytics, hormones, immunoglobulins, sera, thyroid therapeutics, psychopharmaceuticals, antiparkinson agents, other antihyperkinetics, ophthalmologicals, neuropathy products, calcium metabolism regulators, muscle relaxants, lipid-lowering agents, liver therapeutics, coronary agents, cardiac agents, immunotherapeutics, regulatory peptides and their inhibitors, hypnotics, sedatives, gynecologicals, antigout agents, fibrinolytics, enzyme products and transport proteins, enzyme inhibitors, emetics, perfusion promoters, diuretics, diagnostics, corticoids, cholinergics, biliary therapeutics, antiasthmatics, bronchospasmolytics, beta-receptor blockers, calcium channel blockers, ACE inhibitors, arteriosclerosis remedies, antiinflammatory agents, anticoagulants, antihypotensives, antihypoglycemics, antifibrinolytics, antiepileptics, antiemetics, antidotes, antidiabetics, antiarrhythmics, antianemics, antiallergics, anthelmintics, analgesics, analeptics, aldosterone antagonists and weight-reducing agents.

21. An oral dosage form as claimed in claim 17, which is used to produce compressed tablets.

22. A drug product with delayed release of active ingredient, which is an oral dosage form as claimed in claim 17.

23. A drug product for delayed release of active ingredient, which is an oral dosage form as claimed in claim 17 which has been produced by compression.

25. The method of delaying the release of at least one active ingredient comprising producing the oral dosage form of claim 17 wherein the at least one active ingrdient comprises food supplements or additives, vitamins, minerals or trace elements.

27. A process as claimed in claim 1, wherein the production is either continuously or batchwise.

28. A process as claimed in claim 1, wherein the granulated mixture is further processed by forced screening of the granules in the hot state or in the cooled state.

29. A process as claimed in claim 1, wherein the water-soluble polymers are selected from the group consisting of alginates, pectins, galactomannans, carrageenans, dextran, curdlan, pullulan, gellan, chitin, gelatin, xanthans, hemicelluloses, cellulose derivatives, starch derivatives, maltodextrins, polyacrylic acid, polymethacrylic acid, acrylic acid/methacrylic acid copolymers, polyvinyl alcohols, high molecular weight polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers and high molecular weight polyvinylpyrrolidones.

30. A process as claimed in claim 29, wherein the cellulose derivatives are selected from the group consisting of methylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose and carboxymethylcellulose; and the starch derivatives are selected from the group consisting of carboxymethylstarch and degraded starch.

31. A process as claimed in claim 1, wherein the lipophilic substances are selected from the group consisting of fatty alcohols, fatty acids, glycerides, fatty acid esters, fatty alcohol esters and lipophilic polymers.

32. A process as claimed in claim 31, wherein the fatty alcohol is stearyl alcohol; the fatty acid is stearic acid; and the lipophilic polymers are selected from the goup consisting of ethylcellulose, cellulose acetate, acrylic ester/methacrylic ester copolymers, methacrylic acid/acrylic ester copolymers, cellulose acetate phthalate, cellulose acetate succinate, hydroxypropylmethylcellulose acetate phthalate and hydroxypropylmethylcellulose acetate succinate.

33. The dosage form defined in claim 17 which comprises water or solvent in amounts of less than 5% to increase surface moisture.

EVIDENCE APPENDIX:

1) Kolter et al., US 6,066,334
The document was presented with appellants' paper filed February 16, 2006, in reply to a non-final Office action dated September 27, 2005. Although not specifically acknowledged by the Examiner, entry of the document was suggested by the introductory remarks of the subsequent final Office action dated February 27, 2007

2) ***Hawley's*** Condensed Chemical Dictionary, 13th Ed. 1997, page 417
The document was presented with appellants paper filed June 08, 2007, in reply to the final Office action dated February 27, 2007. Although not specifically acknowledged by the Examiner, entry of the document was suggested by the checked box in No. 11 on form PTOL-303 of the Advisory Action dated July 11, 2007, in conjunction with the un-checked boxes in Nos. 8 and 9 of said Action.

RELATED PROCEEDINGS APPENDIX:

NONE